

SUGAR-CONTAINING AMPHIPHILIC OLIGOMERS

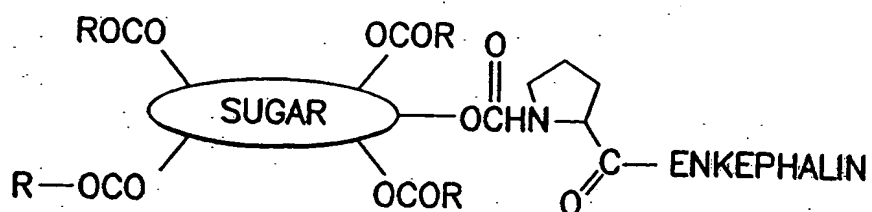


FIG. 1A

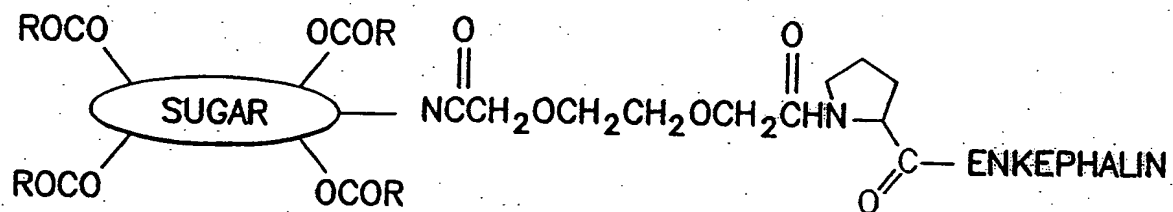


FIG. 1B

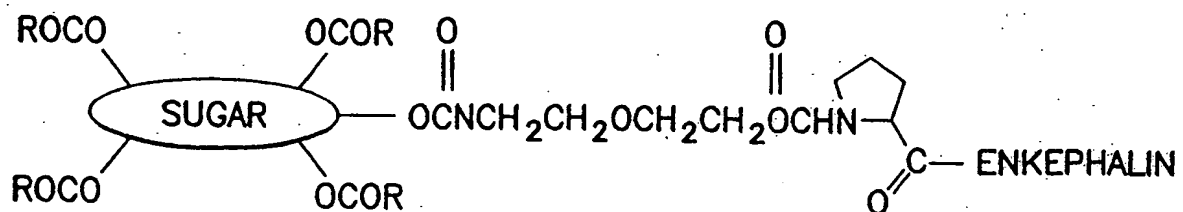


FIG. 1C

STABILITY OF ENKEPHALIN AND CETYL-PEG₂-ENKEPHALIN
IN RAT BRAIN HOMOGENATE

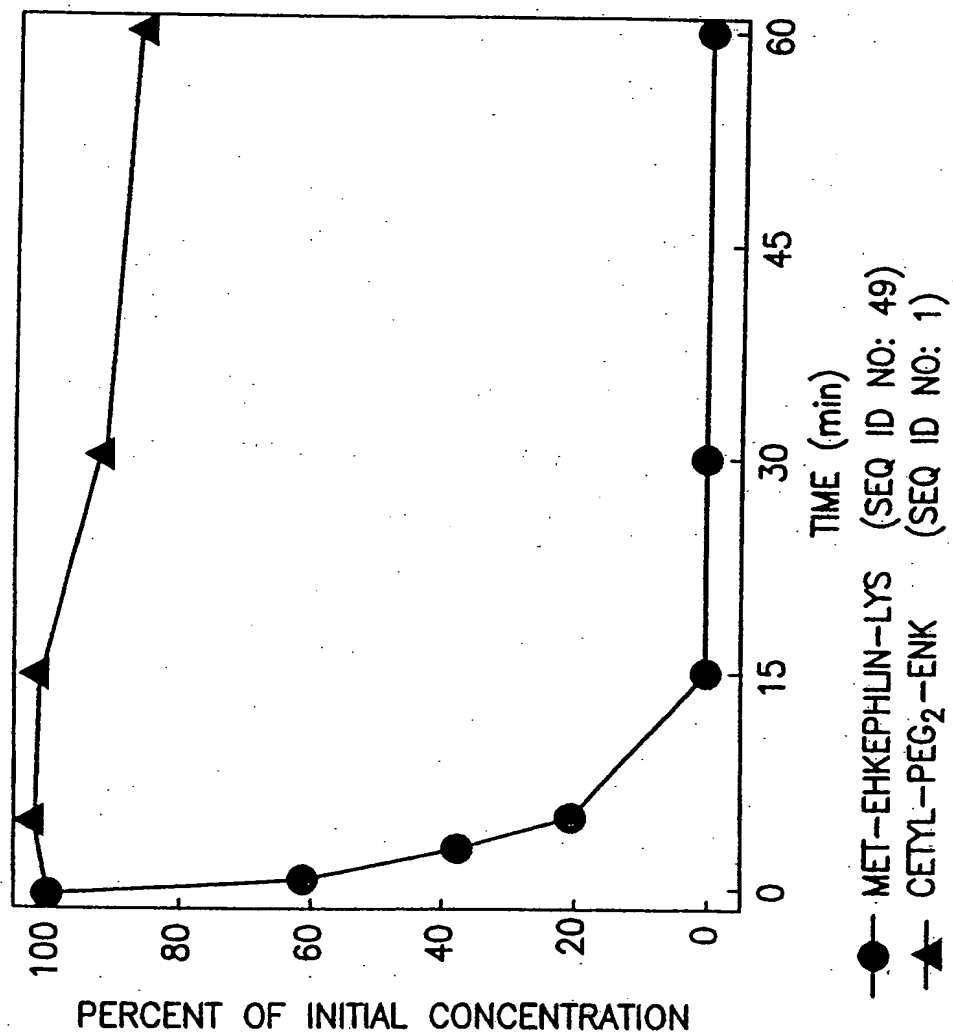
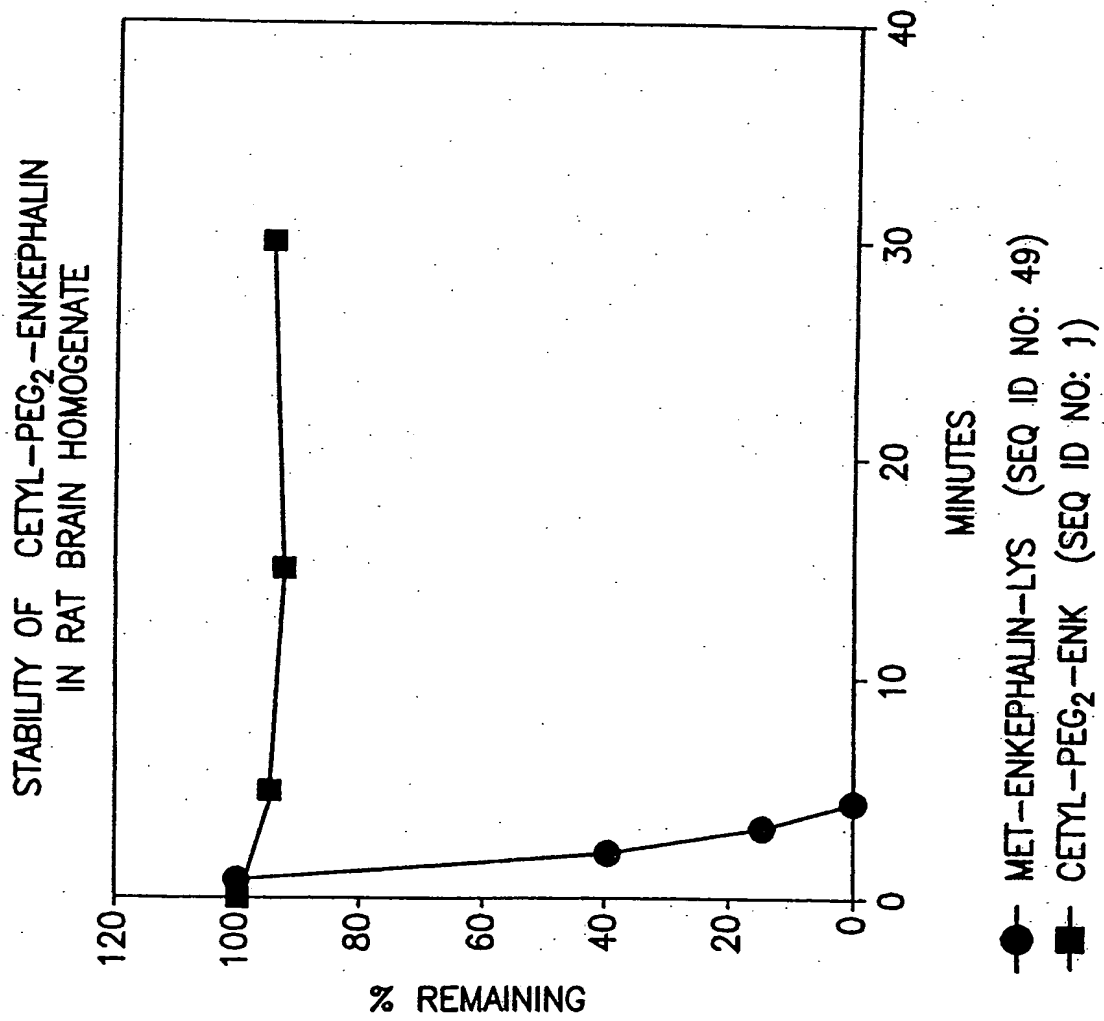


FIG.2

**FIG.3**

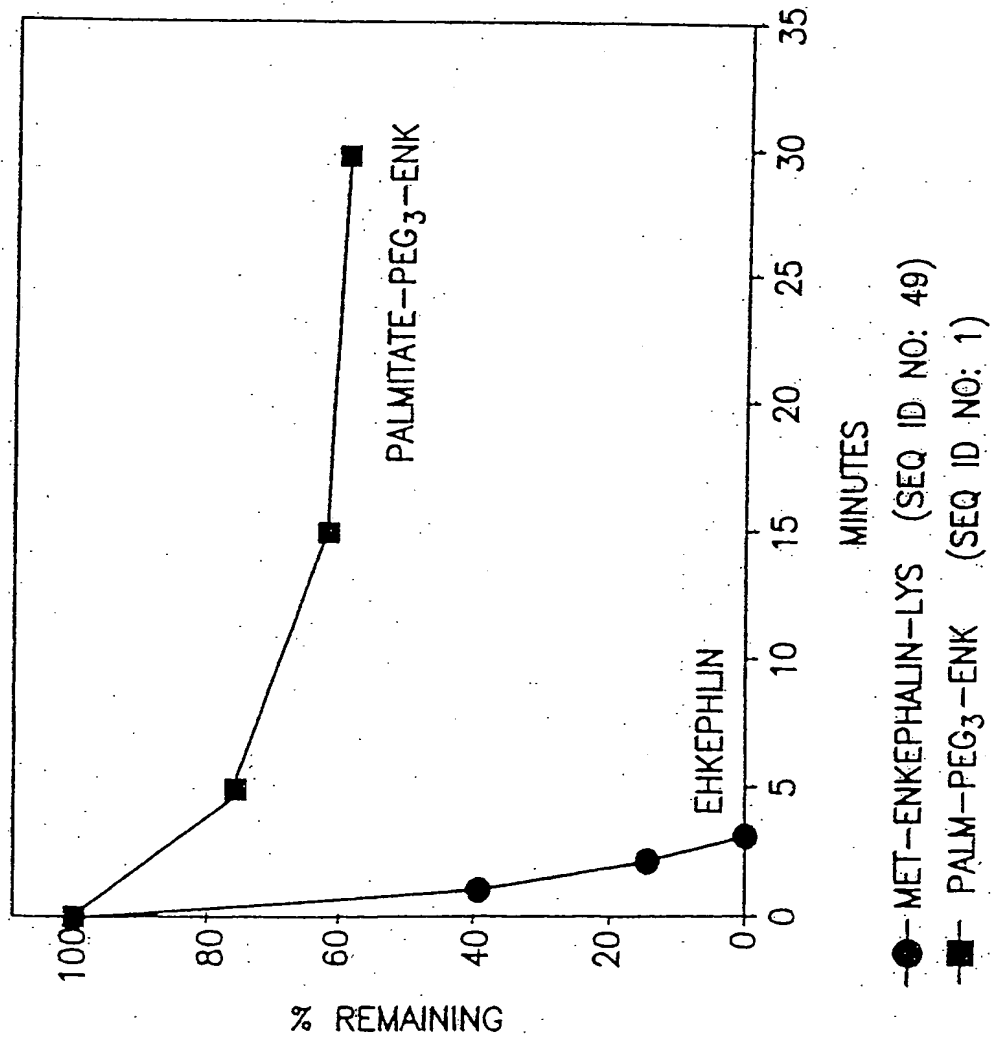
STABILITY OF PALMITATE-PEG₃-ENKEPHALIN
IN RAT BRAIN HOMOGENATE

FIG.4

ISOLATION OF CETYL-PEG₂-ENKEPHALIN (SEQ ID NO: 1) FROM THE BRAIN

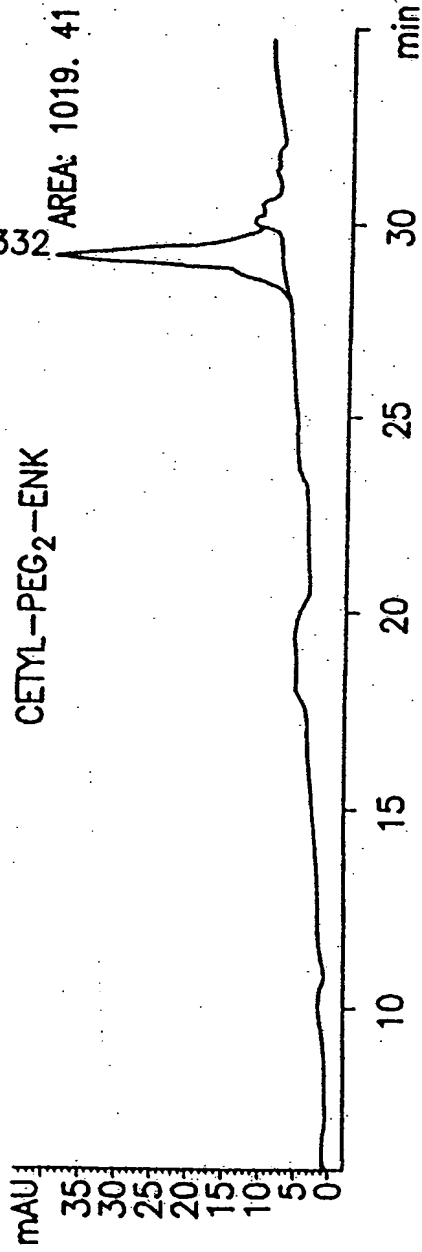


FIG. 5A

CETYL-PEG₂-ENK (SEQ ID NO: 1)

FROM BRAIN EXTRACT

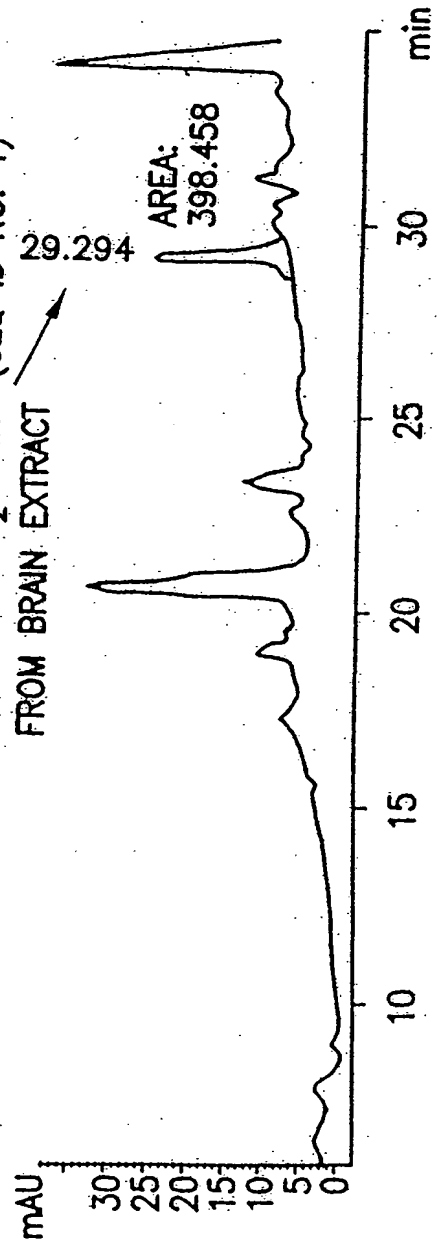


FIG. 5B

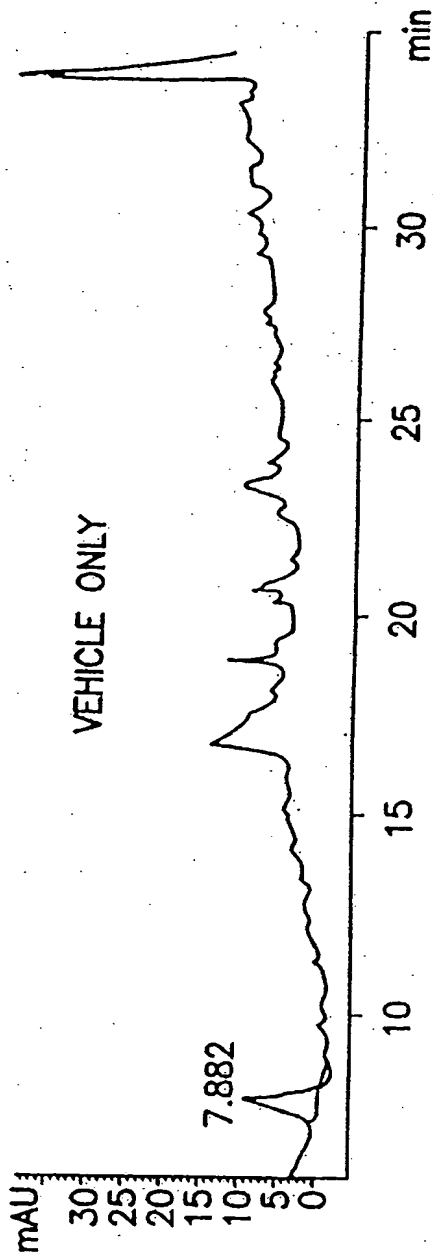


FIG.5C

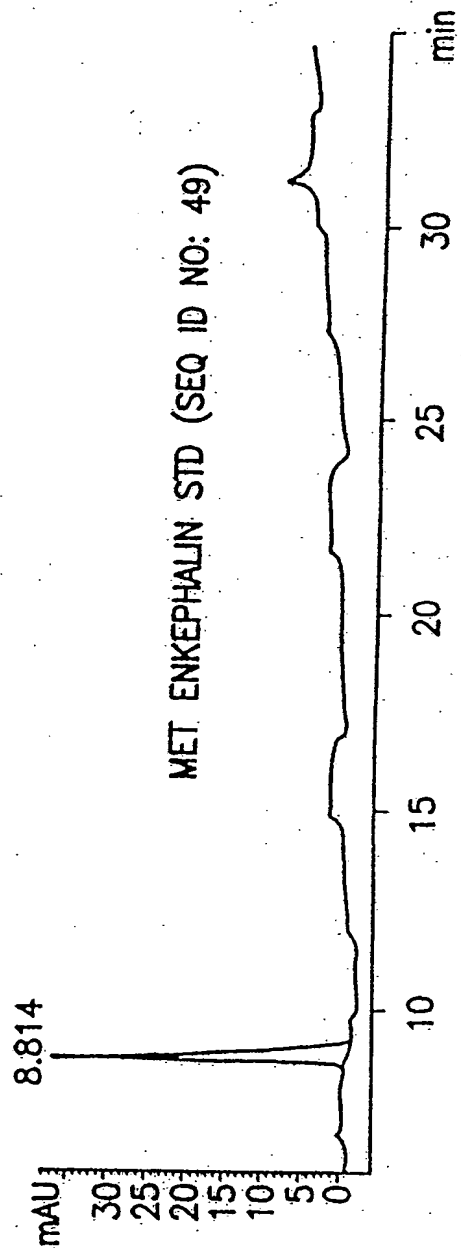
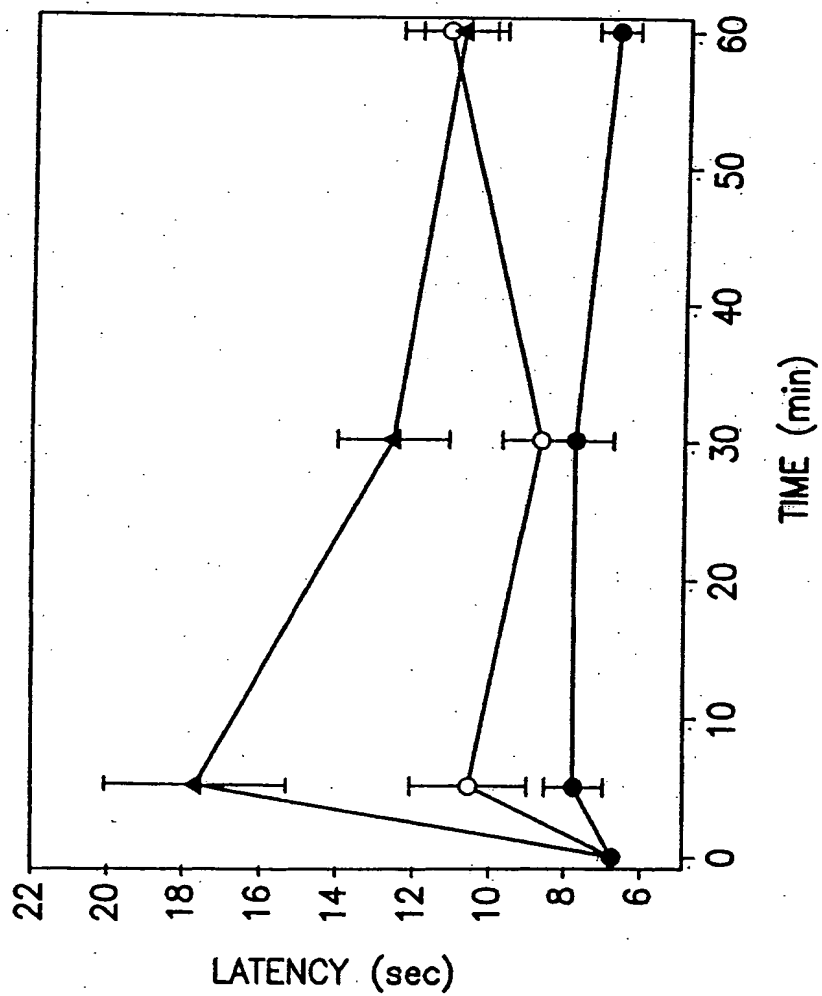


FIG.5D

NALOXONE ANTAGONISM OF
CETYL-PEG₂-ENKEPHALIN-INDUCED ANALGESIA

- NALOXONE
- NALOXONE+CETYL-PEG₂-ENKEPHALIN (SEQ ID NO: 1)
- ▲ CETYL-PEG₂-ENKEPHALIN (SEQ ID NO: 1)

FIG.6

ANALGESIC EFFECT OF A 5 mg/kg IV DOSE OF CETYL-PEG₂-ENKEPHALIN (SEQ ID NO: 1)
MONOCONJUGATE IN THE RAT HOT-PLATE ASSAY

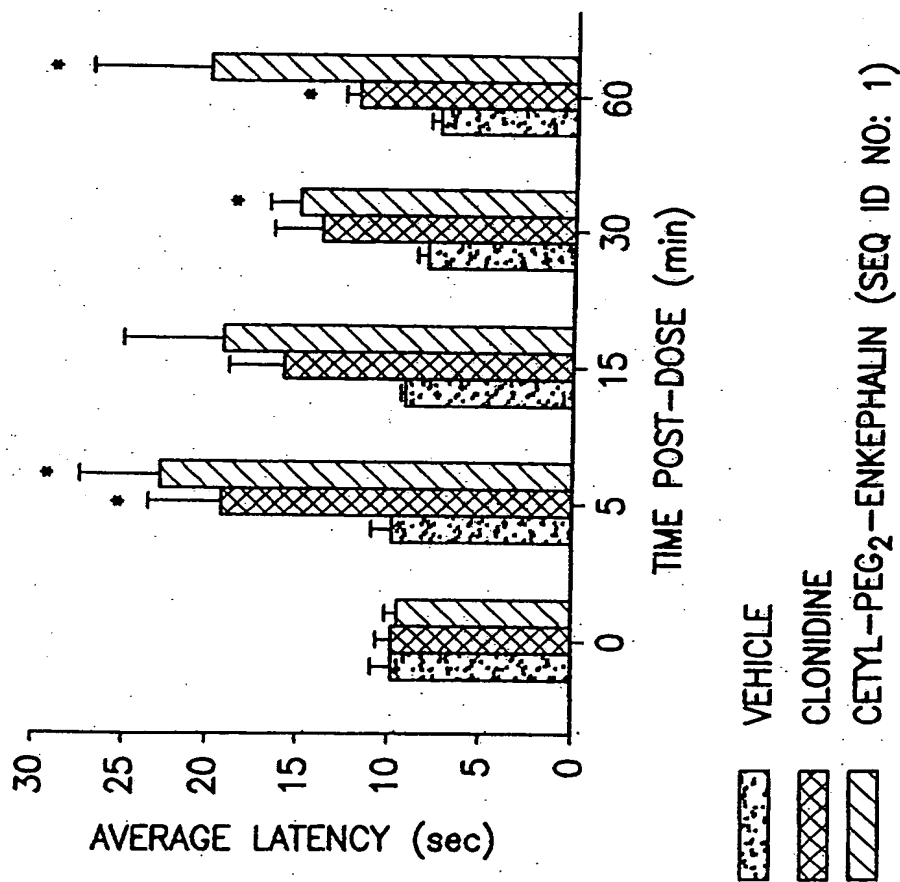


FIG.7

| COMPARISON OF μ -RECEPTOR BINDING AFFINITY OF ENKEPHALIN CONJUGATES | | |
|---|--|--------------------|
| DRUG OR CONJUGATE | DETAILED STRUCTURE | % SPECIFIC BINDING |
| NALOXONE | NALOXONE | 100 |
| ENKEPHALIN | MET-ENKEPHALIN-LYS (SEQ ID NO: 49) | 67 |
| CETYL-ENK | CETYL-PEG ₂ -ENK (SEQ ID NO: 1) | 100 |
| CHOL-ENK | CHOLESTEROL-PEG ₃ -ENK (SEQ ID NO: 1) | 95 |
| DHA-ENK | DHA-PEG ₂ -ENK (SEQ ID NO: 1) | 63 |
| PALM-ENK | PALMITATE-PEG ₃ -ENK (SEQ ID NO: 1) | 76 |
| CETYL-TEG-ENK | CETYL-PEG ₃ -ENK (SEQ ID NO: 1) | 100 |

FIG.8

SYNTHESIS OF OLIGOMER

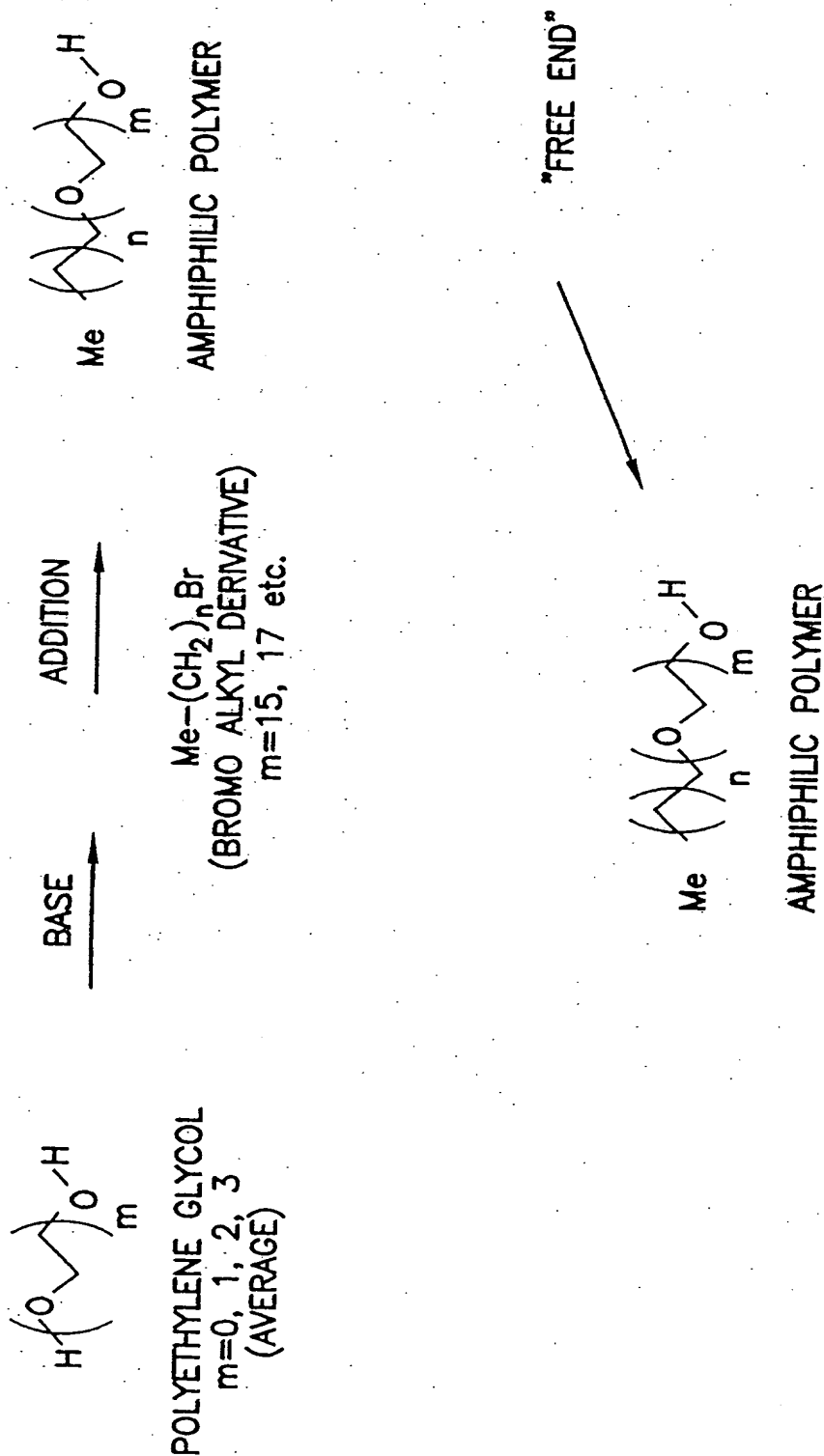
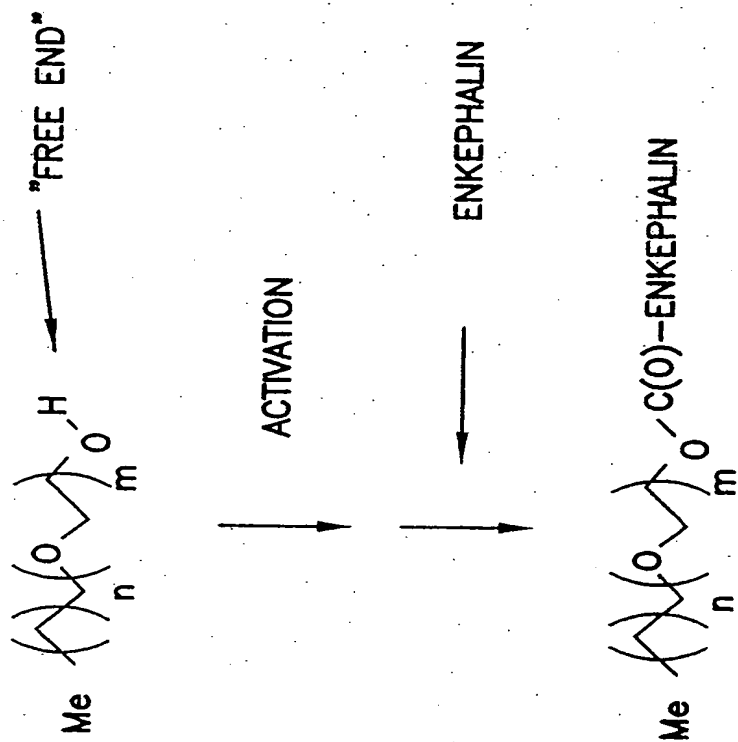


FIG.9

ATTACHMENT OF OLIGOMER TO ENKEPHALIN



OLIGOMER-ENKEPHALIN-CONJUGATE

EXAMPLE $m=14$ AND $n=2$ CETYL-PEG₂-ENKEPHALIN

FIG.10